

Application No. 09/964,215
Amendment dated October 21, 2003
Reply to Office Action of October 6, 2003

Atty Dkt No. 7610-0001.25

AMENDMENTS TO THE SPECIFICATION

On page 1 of the application, please amend the paragraph beginning on line 7 and ending on line 10 as follows (corresponding to paragraph [0001] of the published application, No. 2002/0037527):

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a continuation-in-part of U.S. Patent Application Serial No. 09/727,392, filed November 29, 2000, abandoned, which is a continuation-in-part of U.S. Patent Application Serial No. 09/669,996, filed September 25, 2000, abandoned, the disclosures of which are incorporated by reference herein.

Please amend the paragraph beginning on page 11, at line 20, and ending on page 12, at line 3, i.e., paragraph [0028] of the published application, as follows:

The invention makes use of a focused acoustic energy device as described in U.S. Patent Application Serial No. U09/669,996 ("Acoustic Ejection of Fluids from a Plurality of Reservoirs"), inventors Ellison, Foote and Mutz, filed on September 25, 2000, and assigned to ~~Picoliter, Inc. (Mountain View, California)~~ Picoliter Inc. (Sunnyvale, California). As described in the aforementioned patent application, the device enables acoustic ejection of a plurality of fluid droplets toward designated sites on a substrate surface for deposition thereon, and comprises: a plurality of reservoirs or other fluid-containing means, each adapted to contain a fluid; an acoustic ejector that includes an acoustic radiation generator and a focusing means for focusing the generated acoustic radiation at a focal point sufficiently near the fluid surface in each of the reservoirs such that droplets are ejected therefrom; and a means for positioning the ejector in acoustic coupling relationship to each of the reservoirs. Preferably, each of the reservoirs is removable, comprised of an individual well in a well plate, and/or arranged in an array. In addition, it is preferred that the reservoirs are substantially acoustically indistinguishable from one another.

Please amend the paragraph on page 30, lines 4-26 of the specification, i.e., paragraph [0081] of the published application, as follows:

Moreover, the present methodology may be adapted to eject fluids of virtually any type and amount desired. The fluid may be aqueous and/or nonaqueous. Examples of fluids include, but are not limited to, aqueous fluids such as water *per se* and water- solvated ionic and non-ionic solutions, organic

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solvents, and lipidic liquids, suspensions of immiscible fluids and suspensions or slurries of solids in liquids. Because the invention is readily adapted for use with high temperatures, fluids such as liquid metals, ceramic materials, and glasses may be used; see, e.g., co-pending patent application U.S. Serial No. 09/669/194 ("Method and Apparatus for Generating Droplets of Immiscible Fluids"), inventors Ellison and Mutz, filed on September 25, 2000, and assigned to ~~Picoliter, Inc. (Mountain View, California)~~ Picoliter Inc. (Sunnyvale, California). U.S. Patent Nos. 5,520,715 and 5,722,479 to Ocftering describe the use of acoustic ejection for liquid metal for forming structures using a single reservoir and adding fluid to maintain focus. U.S. Patent No. 6,007,183 to Horine is another patent that pertains to the use of acoustic energy to eject droplets of liquid metal. The capability of producing fine droplets of such materials is in sharp contrast to piezoelectric technology, insofar as piezoelectric systems perform suboptimally at elevated temperatures. Furthermore, because of the precision that is possible using the inventive technology, the device may be used to eject droplets from a reservoir adapted to contain no more than about 100 nanoliters of fluid, preferably no more than 10 nanoliters of fluid. In certain cases, the ejector may be adapted to eject a droplet from a reservoir adapted to contain about 1 to about 100 nanoliters of fluid. This is particularly useful when the fluid to be ejected contains rare or expensive biomolecules, wherein it may be desirable to eject droplets having a volume of about 1 picoliter or less, e.g., having a volume in the range of about 0.025 pL to about 1 pL.

Please amend the paragraph on page 32, lines 1-15 of the specification, i.e., paragraph [0084] of the published application, as follows:

For some applications, especially those involving acoustic deposition of molten metals or other materials, a heating element may be provided for maintaining the substrate at a temperature below the melting point of the molten material, but above ambient temperature so that control of the rapidity of cooling may be effected. The rapidity of cooling may thus be controlled, to permit experimentation regarding the properties of combinatorial compositions such as molten deposited alloys cooled at different temperatures. For example, it is known that metastable materials are generally more likely to be formed with rapid cooling, and other strongly irreversible conditions. The approach of generating materials by different cooling or quenching rates ~~my~~may be termed combinatorial quenching, and could be effected by changing the substrate temperature between acoustic ejections of the molten material. A more convenient method of evaluating combinatorial compositions solidified from the molten state at different

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rates is by generating multiple arrays having the same pattern of nominal compositions ejected acoustically in the molten state onto substrates maintained at different temperatures.

Please amend the paragraph beginning on page 34, at line 23, and ending on page 35, at line 8, i.e., paragraph [0090] of the published application, as follows:

Alternatively, an oligomer may be synthesized prior to attachment to the substrate surface and then "spotted" onto a particular locus on the surface using the focused acoustic ejection methodology described in detail above. Again, the oligomer may be an oligonucleotide, an oligopeptide, or any other biomolecular (or nonbiomolecular) oligomer moiety. Preparation of substrate-bound peptidic molecules, e.g., in the formation of peptide arrays and protein arrays, is described in co-pending patent application U.S. Serial No. 09/669,997 ("Focused Acoustic Energy in the Preparation of Peptidic Arrays"), inventors Mutz and Ellson, filed September 25, 2000 and assigned to ~~Picoliter, Inc. (Mountain View, California)~~ Picoliter Inc. (Sunnyvale, California). Preparation of substrate-bound oligonucleotides, particularly arrays of oligonucleotides wherein at least one of the oligonucleotides contains one or more partially nonhybridizing segments, is described in co-pending patent application U.S. Serial No. 09/699,267 ("~~Arrays of Oligonucleotides Containing Nonhybridizing Segments~~"), inventor Ellson, also filed on September 25, 2000 and assigned to ~~Picoliter, Inc.~~ Picoliter Inc. Preparation of other types of arrays using focused acoustic energy is described in co-pending patent application U.S. Serial No. ~~09/727,392~~ 09/727,392, filed on November 29, 2000 and also assigned to ~~Picoliter, Inc.~~ Picoliter Inc.